UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,832	10/03/2006	**Kazunosuke Aida**	27562U	2366

20529 7590 11/25/2008

THE NATH LAW GROUP
112 South West Street
Alexandria, VA 22314

EXAMINER	
HUANG, GIGI GEORGIANA	
ART UNIT	**PAPER NUMBER**
1612	

MAIL DATE	DELIVERY MODE
11/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,832	AIDA ET AL.	
	Examiner	Art Unit	
	GIGI HUANG	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *11, 13-14, and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 12, 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

Status of Application

1. The response filed August 28, 2008 has been received, entered and carefully considered. The response affects the instant application accordingly:

   a. Claims 1 and 5 have been amended.

2. Claims 1-16 are pending in the case.

3. Claims 11, 13-14, and 16 are withdrawn from examination being drawn to the non-elected invention due to original presentation as addressed in the previous office action.

4. Claims 1-10, 12, 15 are present for examination.

5. The text of those sections of title 35.U.S. Code not included in this action can be found in the prior Office action.

6. All grounds not addressed in the action are withdrawn or moot.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-10, 12, and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to an adhesive comprising a polymer "obtained by" polymerizing two monomers. The first is either vinyl acetate or PVP (N-vinyl-2-pyrrolidone) and the second monomer is a (meth)acrylic acid

alky ester with a C8 alkyl group. However, as it is unclear what the resulting polymers are as polymerization of monomers can result in widely different polymers, even with the same two monomers repeatedly depending on the temperature, amounts, timing, method of making, sequence, additives, and humidity it is vastly unclear what the end product would be even with the same monomers. It does not allow one of skill in the art to ascertain the metes and bounds of the invention. For the purposes of prosecution, any polymers/co-polymers comprising either the monomer vinyl acetate or PVP in conjunction with 2-ethylhexyl(meth)acrylate or octyl(meth)acrylate as these are the only C8 alkyl ester methacrylics clearly addressed (specification page 8).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-10, 12, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tateishi et al. (WO 02/069942) in view of Liedtke (DE 3811564).

It is noted that U.S. Pat. Publication 2004/0096491 will be used as the translation for Tateishi et al. (WO 02/069942). All references will relate to the translation.

It is noted that there is machine translation from the EPO website for Liedtke (DE 3811564). All references will relate to the translation.

Tateishi et al. teaches a transdermal patch comprising a support, an acrylic adhesive layer, and a release paper. The support has a preferred range of 5 to 1000 um and can be formed from different supports including polyethylene terephthalate. The adhesive layer has an adhesive base and a drug wherein the adhesive base comprises an acrylic polymer and a rubber-based polymer sufficiently enhance the permeability of the drug and the penetration properties of the patch (paragraph 12-13). The rubber-based polymer is most preferably either a styrene-isoprene-styrene block copolymer or a polyisobutylene (paragraph 16-17). The acrylic base preferably contains at least one selected from the group consisting of a block copolymer of a polymethyl methacrylate and a polyacrylate containing at least one selected from the group consisting of 2-ethylhexyl acrylate, butyl acrylate, diacetone acrylamide, or tetraethylene glycol dimethacrylate; a 2-ethylhexyl acrylate.N-vinyl-2-pyrrolidone.1,6-hexane glycol dimethacrylate copolymer; an aminoalkylmethacrylate copolymer E; and a 2-ethylhexyl acrylate.vinyl acetate copolymer; and more preferably at least one selected from the group consisting of a 2-ethylhexyl acrylate-N-vinyl-2-pyrrolidone 1,6-hexane glycol dimethacrylate copolymer and a 2-ethylhexyl acrylate.vinyl acetate copolymer.

2-ethylhexyl acrylate-N-vinyl-2-pyrrolidone.1,6-hexane glycol dimethacrylate copolymer and/or 2-ethylhexyl acrylate.vinyl acetate copolymer are preferred and the preferred rubber base polymer is a styrene-isoprene-styrene block copolymer, since they enhance both the skin permeability of the drug and preparation properties (paragraph 16-18, 24, 28, 30-34). These acrylic adhesives are commercially available

and examples are DURO-TAK87-2097 and DURO-TAK87-4098. It is noted that while Tateishi does not specifically recite the typical ranges for the monomers in the adhesive, he does teach that there are no specific restriction on the content of the acrylic polymer, and Tateishi addresses that many of the acrylic adhesives used for this purpose are commercially available such DURO-TAK87-2097 and DURO-TAK87-4098 which are utilized in Tateishi and in the instant specification (see Example 1, and paragraph 24) as a pressure sensitive adhesive. As the components utilized are the same, the monomer mixture would be expected to be the same in both the art and the instant application as they are both the same commercially available product.

Tateishi also teaches that the adhesive can also include a plasticizer. It is noted that the term "obtained by" in claims 1-10 denotes a product by process limitation in which only the end product is the limitation for examination which is addressed in the 112 rejection above. The release paper can be from several materials including polyethylene terephthalate.

Tateishi et al. teaches several specific examples of transdermal patches with the drug pergolide mesylate, DURO-TAK87-4098, styrene-isoprene-styrene block copolymer, plasticizer, and polyethylene terephthalate as the support and the release layer. (Abstract, Page 1, paragraph 12, Page 2, paragraph 14-15 and 20-25, Page 3, paragraph 32-34, Page 5, paragraph 41, Page 6, paragraph 52-53, Page 7, Example 3, paragraph 86-96, Example 4-1, paragraph 98-107).

Tateishi et al. does not expressly teach the incorporation of a cover material or the specific thickness of 12-30um.

Liedtke teaches the improved absorption of medicinal plasters forms with an elastic foam/polymer barrier with polyethylene, an acrylic adhesive, and a flexible barrier from polyethylene, a drug containing layer with a glue layer and the release foil. The advantages of encasing the plaster and having the plaster supported with a foam pad are increased variation, technical simplification, increased durability due to the elasticity and soft consistency, improved contour attachment to the skin surface, and reduced pressure on the skin. This also has improved duration of storage, improved adhesion and better sealing. (Abstract, Paragraph 1, 4-6, 9-11).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to incorporate the foamed polymer, cover layer, and adhesive, as suggested by Liedtke, and produce the instant invention. The increased stability, storage, skin attachment, and durability would be substantial improvements that would create better drug profiles and reduced peeling of the transdermal patch. It would be obvious to also use the same adhesive for the outer layer (e.g. DURO-TAK) as used in the patch taught in Tateishi for simplified production, reduced costs, (no need to produce an additional adhesive), compatibility, and is an acrylate base.

One of ordinary skill in the art would have been motivated to do this because as taught by Liedke, the addition of the cover layer and its components resulted in better skin attachment and durability which is desirable and would improve patient compliance. Increased storage periods are also very desirable for manufacturers as it lower production costs.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to arrive at the thickness of 12-30 um utilizing routine optimization within the ranges taught by Tateishi and produce the instant invention.

It is obvious to vary and/or optimize the thickness provided in the transdermal position, according to the guidance provided by Tateishi, to provide a composition having the desired properties such as the desired (ratios, concentrations, percentages, etc.). Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Additionally, one of ordinary skill in the art would have been motivated to optimize the effective amounts of active ingredients in the composition because the optimization of amounts of active agents to be administered is considered well within the skill of artisan.

One of ordinary skill in the art would have been motivated to do this because it is desirable to adjust the components in a transdermal system to maximize the best possible drug delivery profile and thereby increase market share.

As the structural limitations of the claims are met, the subsequent recited properties are intrinsically met as they would be the same when the composition and the structural recitations are met. A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie

obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. Claims 1-2, 4-7, 9-10, 12, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arth et al. (U.S.Pat. No. 6461636) in view of Terahara et al. (WO 03/013611).

It is noted that U.S. Pat. Publication 2004/0241240 will be used as the translation for Terahara et al. (WO 03/013611). All references will relate to the translation.

Arth et al. teaches a transdermal therapeutic system (TTS) for pergolide and its salts, preferably mesylate. Examples 1-4 are drawn to pergolide mesilate in a TTS comprising a polyester release foil, a matrix mass comprising pergolide mesiliate, a 20um polyester support, a contact adhesive based on crosslinked acrylate copolymers, and then an outer cover of polyurethane encompassing the entire patch to the release film. The adhesives exemplified are of the Euradgit series comprising at least one copolymer of methacrylic acid, acrylic acid, their esters, and variations thereof. Arth also teaches particular materials such as polyacrylate, butyl rubber, and styrene/isoprene copolymers (SIS thereafter) are used in standard pharmaceutical and medical matrices containing active agents (e.g. pergolide mesiliate) (Abstract, Col.2, lines 20-38, Col. 5, lines 35-40, Col. 6, Examples 1-4, lines 45-68, Col. 7, lines 1-44).

Arth et al. does not expressly teach the use of a methacrylic C8 acid ester with vinyl acetate or N-vinyl-2-pyrrolidone or a plasticizer.

Terahara et al. teaches that acrylic adhesives acrylate.vinyl acetate copolymers, 2-ethylhexyl acrylate.2-ethylhexylmetjacrylate.dodecyl methacrylate, and methyl

acrylate.2-ethylhexyl acrylate copolymer are available commercially as the DURO-TAK acrylic series, Eudragit series, and TSR containing N-vinyl-2-pyrrolidone (such as 2-ethyldexyl acrylate.vinylpyrrolidone copolymer solution with1,6-hexaneglycol dimethyacrylate and are analogous and can be combined. Terahara also teaches the inclusion of plasticizers and rubber polymers, preferably styrene-isoprene-styrene block copolymer, in the adhesive and that support layers can be composed of several material including polyurethane, polyethylene, and polyethylene terephthalate (Page 2, paragraph 28-37, Page 3, paragraph 38-42). While Terahara does not teach the specific monomer mixture of 2-ethylhexyl acrylate-N-vinyl-2-pyrrolidone 1,6-hexane glycol dimethacrylate, 2-ethylhexyl acrylate.vinyl acetate copolymer. 2-ethylhexyl acrylate-N-vinyl-2-pyrrolidone.1,6-hexane glycol dimethacrylate copolymer, he teaches that these adhesives are commercially available through the DURO-TAK acrylic adhesive series, and Eudragit ® series. As DURO-TAK87-4098 which is utilized in the instant specification (see Example 1) as a pressure sensitive adhesive and commercially available, the components are the same absent any evidence to the contrary. It is well within the prevue of one in the art to choose any commercial adhesive with the desired properties for the final product. Particularly as these are compatible with drugs of with an ergoline skeleton-the illustrative example is pergolide mesylate (paragraph 29, Examples).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute analogous materials and include plasticizers, as suggested by Terahara, and produce the instant invention. It would have been

obvious to one of skill in the art to try the analogous materials taught, as there are only two other commercial adhesives (DURO-TAK and TSR), that are analogous to Eudragit, and six other support materials other than polyurethane. It is well within the prevue of one in the art to choose any commercial adhesive with the desired properties for the final product. One would add plasticizers, as they are known to improve skin irritation and removal. It would also be obvious to include the SIS to the drug matrix as taught by Arth and Terahara as it provides adhesive properties and are standard in transdermal drug matrixes.

One of ordinary skill in the art would have been motivated to do this because it is desirable for manufacturers to have analogous choices to substitute the adhesives and support materials when motivated by pricing, availability, or desired properties of the in the final product. It is also desirable for manufacturers to add plasticizers as a reduction in skin irritation and improved removal are desirable qualities for patient preference and increasing marketshare.

As the structural limitations of the claims are met, the subsequent recited properties are intrinsically met as they would be the same when the composition and the structural recitations are met. A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie

obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. Claims 3 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arth et al. (U.S.Pat. No. 6461636) in view of Terahara et al. (WO 03/013611) as in claims 1-2, 4-7, 9-10, and further in view of Liedtke (DE 3811564).

The teachings of Arth et al. and Terahara et al. are discussed above.

Arth in view of Terahara does not expressly teach the use of foamed polymers.

Liedtke teaches the improved absorption of medicinal plasters with an elastic foam/polymer barrier with polyethylene, an acrylic adhesive, and a flexible barrier from polyethylene, a drug containing layer with a glue layer and the release foil. The design construction is similar to the one taught by Arth except for the foamed polymer. The advantages of encasing the plaster and having the plaster supported with a foam pad is increased variation, is technically simpler, and increased durability due to the elasticity and soft consistency, improved contour attachment to the skin surface, and reduced pressure on the skin. This also has improved duration of storage, improved adhesion and better sealing. (Abstract, Paragraph 1, 4-6, 9-11).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to incorporate the foamed polymer as suggested by Liedtke, and produce the instant invention. The increased stability, storage, skin attachment, and durability would be substantial improvements that would create better drug profiles and reduced peeling of the transdermal patch.

One of ordinary skill in the art would have been motivated to do this because improved patient compliance through better skin attachment and durability is desirable. Increased storage periods are also very desirable for manufacturers as it lower production costs.

As the structural limitations of the claims are met, the subsequent recited properties are intrinsically met as they would be the same when the composition and the structural recitations are met. A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

13. Applicant's arguments filed August 28, 2008 have been fully considered but they are not persuasive. Applicant asserts that Tateishi et al. (WO 02/069942) in view of Liedtke (DE 3811564) does not teach the combination of monomers in the drug layer, the support film thickness, and a cover. This is not persuasive as addressed above as Tateishi does teach the combination of monomers, a transdermal patch comprising a support, an acrylic adhesive layer, and a release paper wherein the support has a preferred range of 5 to 1000 um which can be routinely optimized by one of skill in the art, and Liedtke address the benefits of advantages of encasing the plaster with a foam

pad including improved contour attachment to the skin surface which would include the sides of the patch taught in Tateishi as it covers the patch. The art meets the composition recitations of the claims. The remainder of the arguments is to the teachings of the references individually in regards to the instant claims. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references.

14. Applicant's arguments with respect to Arth et al. (U.S.Pat. No. 6461636) in view of Terahara et al. (WO 03/013611)have been fully considered but they are not persuasive as Applicant's assertion that there is no motivation to modify the patch of Arth with the teachings of Terahara as it may render the system unsatisfactory for its intended use. This is not persuasive as there is no indication that substitution of analogous materials would render the transdermal patch ineffective, particularly where Terahara et al. teaches that DURO-TAK acrylic series, Eudragit series, and TSR containing N-vinyl-2-pyrrolidone (such as 2-ethyldexyl acrylate.vinylpyrrolidone copolymer solution with1,6-hexaneglycol dimethyacrylate and are analogous and can be combined and are known in the art to be analogous. Terahara also teaches that these adhesives are commercially available and it is well within the prevue of one in the art to choose any commercial adhesive with the desired properties for the final product particularly when motivated by pricing, availability, or desired properties of the in the final product. Additionally, Arth teaches the inclusion of the polyacrylate and SIS

in the drug layer is standard (adhesive components) and is supported by Terahara, the composition limitations are met.

Applicant's argument that the drug containing layer does not migrate into the pressure-sensitive adhesive layer is not persuasive as when the composition recitation of the drug layer is met, the recite properties of the composition are intrinsically met.

Applicant's argument that Arth and Terahara do not teach a cover material is incorrect as Arth et al. teaches a transdermal therapeutic system (TTS) for pergolide and its salts, preferably mesylate. Examples 1-4 are drawn to pergolide mesilate in a TTS comprising a polyester release foil, a matrix mass comprising pergolide mesiliate, a 20um polyester support (is between 13-30um), a contact adhesive based on crosslinked acrylate copolymers, and then an outer cover of polyurethane encompassing the entire patch to the release film.

The remainder of the arguments is to the teachings of the references individually in regards to the instant claims. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references.

15. The arguments with respect to the content of Arth et al. (U.S.Pat. No. 6461636) in view of Terahara et al. (WO 03/013611) and further in view of Liedtke (DE 3811564) have been fully considered but they are not persuasive. The arguments in regards to Arth in view of Terahara are addressed above. The remainder of the arguments is to the teachings of Liedtke individually in regards to the instant claims. In response to applicant's arguments against the references individually, one cannot show

nonobviousness by attacking references individually where the rejections are based on combinations of references.

Conclusion

16. Claims 1-10, 12, and 15 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GIGI HUANG whose telephone number is (571)272-9073. The examiner can normally be reached on Monday-Thursday 8:30AM-6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fredrick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GH

/Zohreh A Fay/
Primary Examiner, Art Unit 1612